Report

Developing Problem Solving Skills in Bioscientists




A report of a workshop for invited participants organised by the UK Centre for Bioscience, Higher Education Academy

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Introduction

Problem solving skills are highly valued by academics and employers. Unfortunately, research supervisors and industrialists frequently indicate that many of our graduates have very poor problem solving abilities; for the majority of our students there would therefore appear to be a need to reach the parts that currently our educational systems fail to reach. It is also important to note that bioscience courses are increasingly taught in a climate of reduced funding per student, increased student numbers and burgeoning subject content. We are therefore faced with the very considerable challenge of developing students' problem solving skills in this difficult environment.

During December 2008, the Centre for Bioscience responded to these challenges by organising a workshop with the theme: 'Engaging Students: What's the Problem'. Seventeen participants, from a range of disciplines and backgrounds, met in Manchester to consider how we might help promote and develop analytical, critical and creative approaches to problem solving in UK bioscience students. Discussions were wide ranging and our speakers and participants considered approaches that might be adopted with problems that extended from algorithmic questions with a single predictable answer to broad, open-ended questions that could be answered in a number of ways.

This report summarises the outcomes of the workshop. The reader will find a summary of the keynote presentation by Tina Overton who set the scene by describing algorithmic, conceptual and open-ended problems and reviewing strategies that may promote students' problem solving skills. There follow brief accounts of the presentations by Kay Hack, Mitch Fry and Paul Ellwood. Kay gave an account of some developments in problem based learning (PBL) with focus on PBL in the teaching of bioinformatics. Mitch described a specific approach to solving more traditional, algorithmic problems while Paul discussed creative approaches to problem solving. In the last session of the workshop, participants worked in groups to consider the key problem solving skills that must be acquired by bioscientists, approaches that may be adopted to promote these skills and issues relating to assessment of problem solving. The report contains summaries of these sessions along with a series of observations and recommendations that stemmed from the discussions. Finally, some of the workshop participants contributed case studies and short exercises that provide clear illustrations of how a number of the issues associated with problem solving in the biosciences may be addressed.

It is beyond the scope of this short report to provide a comprehensive account of problem solving in all of the many bioscience disciplines. Nonetheless, we hope that this document provides a taster of what is currently happening in bioscience and that ultimately it will form the basis of a more extensive resource in support of the development of problem solving skills in our community.

The key problem solving skills that must be acquired by bioscientists

There was some discussion of subject-specific problem solving skills in the biosciences and, in particular, the need to identify and highlight difficult concepts associated with solving problems in the individual disciplines. For example, biochemistry students frequently struggle with the difference between a concentration (e.g. mM) and an amount (e.g. mmole). Similarly, microbiologists need to develop a proper understanding of scale at the microscopic level. Challenging issues of this nature should be addressed as part of the current initiative as colleagues, working in a wide range of bioscience disciplines, devise new problem solving exercises. Looking beyond subject specific elements, a number of key generic skills that students should develop when solving problems in the biosciences were identified:

- ***Problem interrogation*** Identify crucial information and data, and filter-out extraneous material.
- ***Common sense and realism*** As the problem is solved constantly reassess whether the answers make sense by making general estimates of the nature and scale of the likely solution.
- ***Statistics*** Related to 'Common sense and realism', develop an understanding of significance testing and confidence intervals.
- ***Data analysis*** Learn how to analyse numerical information summarised in figures and tables. Develop analytical skills that allow data to be transformed and presented in formats that yield the maximum amount of information.
- ***Time management*** If there is a time limit, plan how the problem may be solved in the time available.
- ***Creativity*** When problems are 'open-ended' adopt creative approaches to problem solving.
- ***Incubation and reflection*** Take time to understand and appreciate the skills that have been acquired.

Additional skills can be developed during problem solving. These include:

- ***Research skills*** Where appropriate, learn how to search the literature to find the information required to solve a problem.
- ***Group work*** Adopt role(s) during a team approach to problem solving; students should learn how to assess their own contributions and those of others.

Promoting problem solving skills

- ***Language*** Poorly phrased questions can cause serious problems for many students, particularly those for whom English is a second language. Avoid this by ensuring that language is precise and unambiguous, that definitions are described clearly and that jargon is eliminated.
- ***Units, amounts, concentrations etc.*** Units of measure (e.g. µmol vs. µM, µm vs. mm) can cause unnecessary confusion and students can fail to answer a question simply because they lack an understanding of, for example, the difference between a concentration and an amount. One way to avoid this is to confront the issue at the beginning of the problem so that students are obliged to consider the nature of units used during the remainder of the exercise.
- ***Reinforce skills and build confidence*** It was agreed that there is little value in asking students to solve single problems in isolation. Instead they should be asked to solve a series of problems that develop and reinforce the specific skills outlined earlier, and build confidence. The 'fading' problem solving approach, where students make a gradual transition from fully worked examples to problems where some elements are in the form of worked examples to problems they must solve independently, may also prove useful in this regard.
- ***Place problems in context*** Wherever possible try to place problems in the context of material being taught elsewhere in the course. Problem solving, as part of an enquiry based approach to laboratory teaching, can prove particularly effective.
- ***Time constraints*** To reflect accurately the different sorts of problems students will be asked to solve in the

world of work, create exercises that require a range of times (e.g. anything between one hour and one week) for completion.

- ***Team work*** Ensure students are given the opportunity to work closely and cooperatively with their peers in team approaches to problem solving. Encourage students to adopt a range of roles within teams.
- ***Embed problem solving within programmes*** Build problem solving exercises and approaches into programmes from the earliest stage and include these in most, if not all, modules. Once again, this should help reinforce skills as students progress from Levels 1-3.
- ***Support from tutors*** Wherever possible, modules should include tutorials and/or workshops that provide continuous and effective support during problem solving.
- ***Reflection*** Students should be encouraged to reflect on the problem solving and other skills they acquire and record their observations in a learning log.
- ***Create new resources: interactive software*** Develop software that facilitates a clear and consistent approach with interactivity, hints and instant feedback during problem solving.

Assessment of problem solving skills

- ***Range of assessment procedures*** Clearly the assessment procedure adopted will depend on the nature of problems (e.g. algorithmic, open ended) being solved.
  a) ***Time allowed*** The amount of time allowed for each assessment will vary markedly. It was considered appropriate to assess both students' capacity to solve a problem under time pressure, e.g. during an end of module exam, and their ability to solve an open-ended problem over a much longer period.
  b) ***Open exams*** Open exams, with a degree of supervision and with students given access to various materials, will be appropriate for some types of problem. The so-called 'Triple Exam' format may prove particularly useful. In the first stage of this approach students are presented with a problem in the classroom. They are asked questions about the problem but they are also encouraged themselves to ask questions, formulate hypotheses and consider additional information they may require to address the issues and solve the problem. Their performance at this stage is assessed. In the second stage students are given time (perhaps overnight) to research the problem by accessing and consulting additional resources. Finally, students return to the classroom where they are asked additional and more difficult questions relating to the original problem; their responses are assessed. The students should now be much better informed and their answers should reflect a greater insight and understanding of the problem/phenomenon under investigation.
- ***Collusion during problem solving*** It was agreed that students must be given the opportunity to solve open ended questions in their own time. However, inevitably, in any form of group work collusion will be an issue and it was also accepted that students are likely to assist one another when completing problem solving assessments that form part of coursework. This seems inevitable and may even prove beneficial as students help one another to develop problem solving skills. However, the opportunity for collusion should perhaps be reflected by the degree of weighting placed on open ended problem solving exercises assessed summatively.
- ***Peer assessment*** Group exercises involving a team approach to problem solving provide excellent opportunities for peer assessment. There are clear benefits associated with this approach which should be encouraged wherever possible.
- ***Feedback and group discussions*** It was agreed that timely feedback is of paramount importance. Students will benefit not only from feedback from tutors but also from discussion with their peers. This could be facilitated in group sessions in which students share their experiences of problem solving with their classmates.

Conclusions and recommendations

The main purpose of this workshop was to find ways to promote and develop creative, analytical and critical approaches to problem solving in the biosciences. A wide range of take home messages emerged from the presentations by our speakers, the detailed discussions involving workshop participants and the case studies/problems that form part of this report. These can be summarised in the following list of key recommendations:

- When designing problems ensure these foster the key/core skills listed on page 2
- Promote problem solving skills using the procedures described on page 2. Briefly:
  a) ensure language is clear and unambiguous
  b) avoid unnecessary confusion associated with units of measure
  c) allow plenty of opportunity for reinforcement of skills
  d) wherever possible place problems in a useful and realistic context
  e) encourage team work during problem solving
  f) ensure an effective backup system is in place to provide regular support
  g) encourage students to reflect on skills acquired using a learning log
  h) create interactive software in support of problem solving
- Use a wide range of assessment procedures and ensure that effective feedback is provided for all problem solving exercises (page 3)

A further point is that it may prove useful to carry out an audit of current teaching practice regarding problem solving in individual institutions. This would provide a baseline for evaluation of students' problem solving abilities before and after implementation of new initiatives stemming from this report.

Some of the above recommendations are ambitious. For example, the creation of interactive software will require a coordinated approach with the provision of materials by practitioners from a wide range of bioscience disciplines. Furthermore, if we are to make significant progress in this area, we will need the support of senior colleagues in institutions who may need to re-think their whole approach to problem solving and perhaps make much more space for problem solving exercises in their curricula. These challenges are not insurmountable and ought to be met given the very considerable rewards to be gained as students become competent and confident problem solvers in a wide range of academic and industrial settings.

Problem solving – strategies, solutions and successes

Tina Overton

The concept of 'graduateness' has often been described in terms of the development of intellectual or higher order cognitive skills (HOCS)(Zoller, 1997). These higher order cognitive skills include problem solving (Terenzini, 1995 and Garratt *et al.,* 2000).

Hayes (1980) postulated that *'whenever there is a gap between where you are now and where you want to be and you don't know how to find a way to cross that gap, you have a problem'*. Johnstone (1993) categorised problems according to three factors; whether data was given, whether the method was familiar, and whether the goals of the problem are well defined. Using this model Johnstone identified eight types of problem ranging from purely algorithmic to completely open.

The influence of cognitive style on student success has been investigated in relation to algorithmic problem solving in chemistry (Johnstone and El-Banna, 1986; Stamovlasis, 2005). This study used the information processing model (Shiffrin, 1977 and Johnstone, 1997). Information processing is an attempt to suggest mechanisms for learning and working memory space is key to processing. However, working memory space (Baddeley, 1986) has a finite capacity in each individual and we can consequently handle only a limited amount of information at any time. Consequently, the demand of a problem in terms of pieces of information, or steps, is crucial in determining success (Johnstone and El-Banna, 1986). Cognitive overload can occur if problems are complex or contain extraneous information that is not essential to the problem. Cognitive overload is minimised by careful design of problems. Strategies include presenting required prior knowledge before presenting the problem, removing 'noise' from the problem, by scaffolding learning by breaking down the problem into smaller steps, and by moving students gradually from worked examples to solving problems.

Renkl *et al.,* (1996), have stated that learning should be motivated by problems that have a real-life context, be authentic, complex and ill-defined. For chemistry, Johnstone (1991) has stated that the subject exists in three forms which can be thought of as corners of a triangle and each form complements the other. These forms of the subject are the macro and tangible, the submacro: atoms, molecules, ions and structures; the *representational* symbols, formulae, equations, etc. He argues that we encounter life on the macro level and that, chemistry, to be more fully understood, has to move to the submicro situation where the behaviour of substances is interpreted in terms of the unseen and molecular and recorded in some representational language and notation. Where this approach has been changed to set learning and problem solving within a real-life context evidence has demonstrated that students engage much more enthusiastically with their learning, (Reid, 2000, and Belt et al., 2002).

The use of additional context can make a problem more engaging but can make it more complex, enhancing the load on working memory. The ability of an individual to pull out relevant information from a complex problem is called field dependence or independence (Witkin, 1981). Field Dependence/Independence is a determining factor in academic achievement. A student who is field dependent has difficulty separating relevant information from irrelevant information or 'signal from noise'.

All these factors should be considered when designing problems for undergraduates.

References

Baddeley A.D. (1986) *Working Memory*. Oxford: Clarendon Press

Belt S.T., Evans E.H., McCreedy T., Overton T.L. and Summerfield S. (2002) A problem based learning approach to analytical and applied chemistry. *University Chemistry Education*, **6**, 65–72

Garratt J., Overton T., Tomlinson J. and Clow D. (2000) Critical thinking exercises for chemists: Are they subject-specific? *Active Learning in Higher Education*, **1**(2), 152–167

Hayes J.R. (1981) *The Complete Problem Solver*. Philadelphia: Franklin Institute Press

Johnstone A.H. and El-Banna H. (1986) Capacities demands and processes: a predictive model for Science Education, *Education in Chemistry*. **23**, 80–84

Johnstone A.H. (1991) Why is Science Difficult to Learn? Things are seldom what they seem. J*ournal of Computer Assisted Learning*, **7**, 75–83

Johnstone A.H. (1993) in Wood C , *Creative Problem Solving* London: Royal Society of Chemistry

Johnstone A.H. (1997) Chemical Education Science or Alchemy? *Journal of Chemical Education*, **74**, 262–268

Reid N. (2000) The presentation of chemistry: logically driven or applications led? *Chemistry Education:Research and Practice in Europe*, 1 (3), 38–392

Renkl A., Mandl H. and Gruber H., (1996) Inert knowledge: Analyses and remedies. *Educational Psychologist*, **31** (2), 115–121

Shiffrin R.M. and Schneider W. (1977) Controlled and automatic human information processing: II. Perceptual learning, automatic attending and a general theory. *Psychological Review* **84** (2), 127–190

Stamovlasis D., Tsaparlis G (2005) Cognitive variables in problem solving: a nonlinear approach. *International Journal of Science and Mathematics Education*, **3** (1) 7–32

Terenzini P.T., Springer L., Pascarella E.T. and Nora A. (1995) Influences affecting the development of students' critical thinking skills. *Research in Higher Education*, **36** (1), 22–39

Witkin H.A. and Goodenough D.R. (1981) Cognitive styles: essence and origins. Field dependence and field independence. Psychololgy Issues, **51**, 1–141

Zoller U. and Tsaparlis G. (1997) Higher and lower-order cognitive skills: The case of chemistry. *Research in Science Education*. **27** (1), 117–130

Delivering bioinformatics - The PBL approach

Catherine Hack

Introduction

Life science course teams are currently faced with the problem of including Bioinformatics into an already crowded curriculum (Hack and Kendall (2005). For the students on these programmes, Bioinformatics is primarily the use of computing tools which allow the management, visualisation, integration and analysis of biological data. The increased availability of software, based on ever more complex algorithms, raises issues around the delivery of bioinformatics education (Hack and Kendall (2005), however at University of Ulster we feel that the aim should be to provide students with an understanding of how bioinformatics can be used to solve problems in the life sciences. In this paper we evaluate the use of a problem based learning approach to deliver bioinformatics education to final year biomedical science and pharmacology students.

Pedagogical background

Problem based learning (PBL) was used to deliver bioinformatics education to final year biomedical science and pharmacology students, as part of a module in Human and Molecular Genetics. It was envisaged that at the end of this period students would be able to take a DNA sequence, and identify some or all of the following: Which gene it came from? Which protein it coded for? What was the protein function? What was the protein structure? What can go wrong?

PBL Scenario

The students were provided with the following problem:

"You are working in a Genetic Screening Laboratory which analyses DNA. You have been provided with a sample of foetal DNA. Please prepare for a meeting with the prospective parents".

Pedagogic Elements

The students (n=59) were randomly assigned to groups of 6. The exercise included 2 classroom sessions, with one lecturer and one facilitator, plus a final role play and review session. The students had 3 weeks to complete the task. Marks were allocated for:

- Participation in group work (peer assessment)
- Role play (peer and tutor assessment)
- Supporting material (tutor assessment).

Examples of Student responses

The students were asked to disseminate their findings using a medium appropriate for their target audience. This open assessment structure resulted in the production of a diverse range of materials, including the following:

- Scientific reports detailing results
- Patient information leaflets
- Posters suitable for Health Centre waiting rooms

They also participated in role play exercises taking on roles as Genetic Counselor, Biomedical Scientist, Clinician etc.

Feedback

The PBL approach was evaluated using student feedback through questionnaires, as well as analysis of coursework and examination results. Analysis of coursework results indicated that there was no significant difference in student performance; i.e. the results that students attained in their PBL assignment were similar to those achieved in other assessments. Students found the PBL learning environment both more enjoyable and more demanding, and increased their interest in the module content. They reported that it helped to develop their key skills compared with traditional teaching methods.

Conclusions and Further Work

The identification of problem scenarios that engage the whole cohort whilst challenging the most able students is critical to the successful implementation of the PBL delivery approach. PBL should be designed such that the student is required to actively process information and utilise prior knowledge; whilst the problem is set in a meaningful context and provides opportunities for development and organization of knowledge. In general, the key features of good PBL scenarios are that they are based on real problems of relevance to the course or module objectives; that they should be open-ended and multi-stage; and they require a range of resources, including personal resources such as skills and knowledge, as well as external resources such as team members, electronic resources and facilitators.

The problem presented here has some limitations in that there was effectively only one way to solve the problem. However whilst all groups completed all the subject specific tasks detailed in the introduction, groups did place differing emphasis on each element and some of the stronger students explored in more depth the probabilities and consequences of mutations. As well as the subject specific skills developed in this exercise the students also developed their key skills in communication, time management, team work, resource finding.

Whilst a wide range of academic disciplines have been delivered using PBL, we believe that it is particularly appropriate for bioinformatics given the extremely dynamic nature of this field. We have received funding under the Centre for Bioscience Teaching Development Fund to facilitate the integration of Bioinformatics into taught undergraduate programmes. We hope to achieve this through the provision of an online resource of 'problem-based scenarios', which can be used and reviewed by the teaching community[1]; we hope this resource will encourage other practitioners to explore the use of PBL to deliver Bioinformatics education

Hack and Kendall (2005a) Bioinformatics: Current practice and future challenges for life science education, *Biochemistry and Molecular Biology Education*. **33** (2) 82–85

Hack and Kendall (2005b) Bioinformatics Education in the UK: Are we educating scientists or training technicians? *Bioscience Bulletin*, **15**, Summer 2005

[1] http://samsara.scic.ulst.ac.uk/-Problem-Based-Learning-.html and http://samsara.scic.ulst.ac.uk/~kay/cgi/pbl.cig

A traditional, multi-step approach to problem solving

Mitch Fry

A traditional, algorithmic approach, to problem solving is described. In this approach an area of study is introduced, appropriate data provided, and student tasks and objectives listed. A full solution to the problem is ultimately made available. The rationale here is that students, once provided with the data, are expected to come to a rational explanation, either independently, as a group, or with the tutor. It is a simple, well-tried and flexible approach to problem solving. Some of the advantages of this approach include:

- The problem provided is very 'in context' with the discipline; to the student it is therefore perceived (correctly so!) as relevant to their studies.
- The data provided may be fabricated, 'wet' i.e. obtained from a laboratory exercise, or acquired by the student from another source, e.g. literature search.
- The 'exercise' is readily assessed.
- The approach is very adaptable. It can be used in a laboratory session (to acquire data or as a supplementary/related exercise), in a tutorial group session, as a practice exercise for a (exam) data handling question, or as an online exercise.
- Feedback to the student is readily provided.
- It reinforces academic knowledge.
- It reinforces key skills of deduction.
- The exercise itself can be 'simple', i.e. suitable for level 1, or can be extended to be more challenging.

This, and similar approaches, have been used for many years in Biochemistry teaching at Leeds, primarily as supplementary exercises in laboratory classes, and within a tutorial group scenario.

Further developments will take this online. It lends itself readily to delivery through software such as QuestionMark Perception (QP); the provision of such online material, with the ability to set, time, record results, and provide instant feedback, is a powerful medium, and one which is generally well received by students. Used appropriately, it also helps students plan and manage their own learning more effectively. Provision of such material can also be made available through the QP community.

The use of Molar Absorption Coefficients in the quantitation of mixtures

The problem

Introduction and setting

Spectrophotometry can provide a direct method for analysing the type and concentration of biological molecules in solution, using the Beer-Lambert Law and the molar absorption coefficient.

The Beer-Lambert equation is:

$A = \varepsilon cl$

ε is the molar absorption coefficient of the compound; it is the light absorption (at a stated wavelength) of a 1 molar solution of the compound. c is the molar concentration of the compound, and l is the light path (in cm) of the containing cuvette, usually 1.

This analytical approach is often restricted however to situations where it is known that other components in the mixture do not absorb radiation at the wavelength used to detect a particular test compound.

Setting the problem

You are provided with an absorption spectrum for a mixture of ATP (adenosine triphosphate) and NADH (nicotinamide adenine dinucleotide) and must calculate the concentration of both species in the mixture. Both compounds absorb radiation at 260nm but only NADH in this solution absorbs radiation at 340nm.

The data

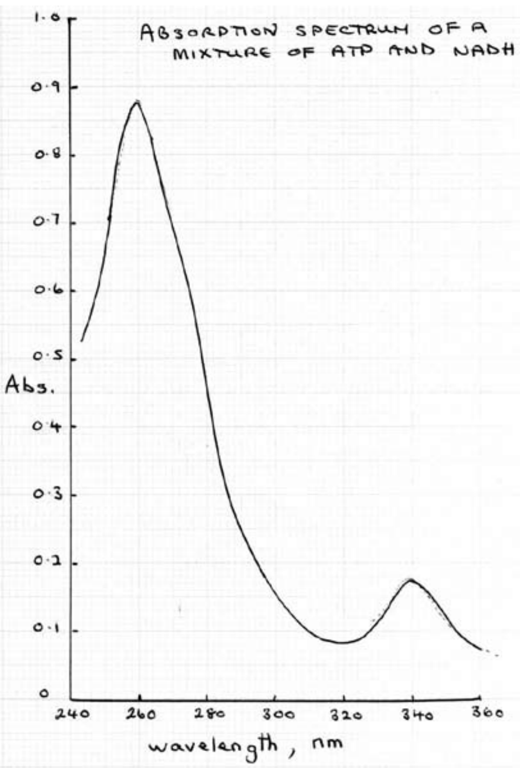


Figure 1: Absorption spectrum of a mixture of ATP and NADH

The molar absorption coefficients for NADH, NAD^+ and ATP are:

		M^{-1} cm^{-1}
NADH	340nm	6200
NAD^+ & NADH	260nm	18000
ATP	260nm	15400

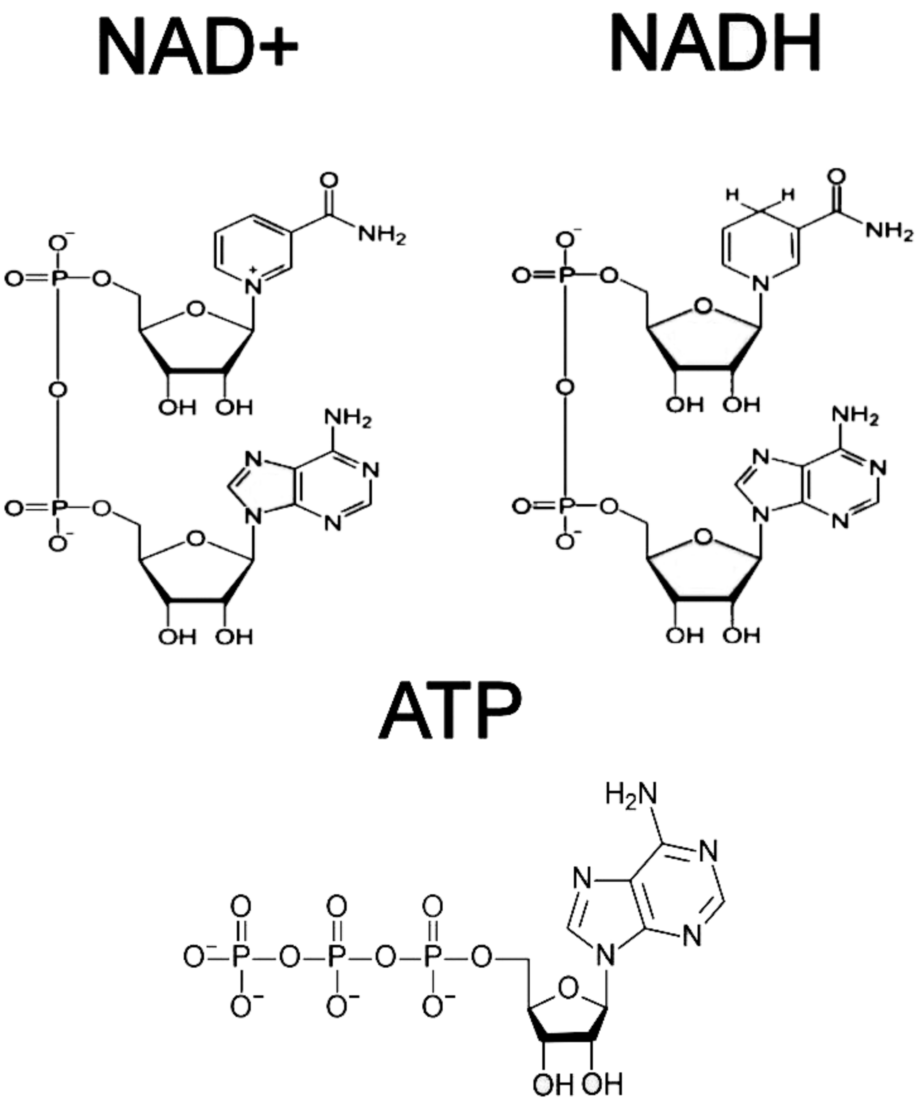


Figure 2: Structures of NAD^+, NADH and ATP

Tasks and Objectives

1. Given the structures of ATP and NADH, explain the absorption spectrum with respect to those chemical components that absorb radiation at 260 and 340nm.
2. Use the absorption spectrum and information given to calculate the concentration of both ATP and NADH in the mixture.

Hints:

1. Consider the similarities and differences in the structures of ATP and NADH; both ATP and NADH absorb radiation at 260nm, but only NADH absorbs radiation at 340nm.
2. Using the Beer-Lambert Law, and given the molar absorption coefficient for NADH at 340nm, calculate the concentration of NADH in the mixture.
3. Using the molar absorption coefficient for NADH at 260nm, rearrange the Beer-Lambert equation to calculate the absorbance contribution at 260nm due to the NADH.
4. By subtraction, calculate the absorbance contribution at 260nm due to the ATP, and hence use the Beer-Lambert equation to calculate the concentration of ATP in the mixture.

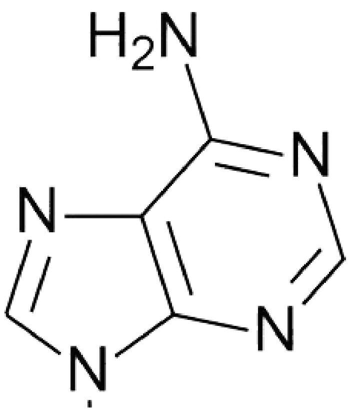
Complete this exercise before turning to …………… The Solution

Analytical

The use of Molar Absorption Coefficients in the quantitation of mixtures

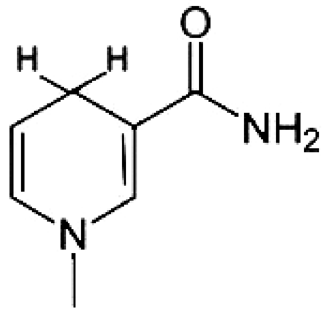
The Solution

Both ATP and NADH have an adenine ring structure in common;



The adenine ring

Since both compounds absorb radiation at 260nm, we can assume that it is this structure that is responsible. In addition, NAD^+ and NADH contain a nicotinamide ring structure; this structure is not present in ATP and in its reduced form (i.e. in NADH) must be responsible for absorption of radiation at 340nm.



The nicotinamide (reduced) ring

No other structures in either of these two molecules would absorb radiation in the wavelength range we are using [*The sugar ribose ring is common to all structures but does not absorb light radiation in this wavelength range*].

Given the uniqueness of the NADH structure and its absorption of radiation at 340nm, we begin by using this information to calculate the concentration of NADH in the mixture.

Using the Beer-Lambert equation:

$A = \varepsilon cl$,   A = 0.18 at 340nm; ε = 6200 M^{-1} cm^{-1} for NADH and l = 1cm.

Rearranging to find the unknown c,

c = 0.18 / 6200 x 1

= 2.9 x 10^{-5} M

[*c is expressed in Molar since we are using a molar absorption coefficient!*]

Now, we can calculate the NADH contribution to the absorbance at 260nm. We need to find the absorption due to NADH at 260nm.

Therefore, using the molar absorption coefficient of NADH at 260 nm:

$A = \varepsilon cl$ = 18000 x 2.9 x 10^{-5} x 1

A = 0.52

Reading from the spectrum, the total absorbance at 260nm is 0.88, therefore 0.88 – 0.52 (=0.36) must be the absorption due to the ATP, at 260nm.

We can now find the concentration of ATP in solution:

0.36 = 15400 x c x l

c = 0.36 / 15400

= 2.3 x 10^{-5} M

In conclusion, the concentration of ATP in the mixture is 2.3 x 10^{-5}M, and the concentration of NADH in the mixture is 2.9 x 10^{-5}M.

Commentary

This exercise is a piece of detective work!

- Being told that only NADH absorbs light radiation at 340nm, and by a process of elimination, we were able to assign the adenine ring as responsible for absorption at 260nm.
- Using the unique properties of NADH absorption at 340nm, we were able to use the data to calculate the concentration of NADH in the mixture.
- By rearrangement of the Beer-Lambert equation we were able to calculate the contribution of NADH to the absorbance at 260nm, and therefore by subtraction that due to the ATP.
- This finally allowed a calculation of the ATP concentration in the mixture.
- With the information found, we could also (if we so wished) double-check the concentration of NADH in the mixture using the absorption coefficient at 260nm.

$A = \varepsilon cl$

$0.52 = 18000 \times c \times 1$

$c = 2.9 \times 10^{-5}$ M (the same result we found using the NADH molar absorption coefficient at 340nm).

NADH is a coenzyme in a number of oxidation-reduction reactions. The fact that only the reduced form absorbs light radiation at 340nm is an important and very useful property of this molecule, enabling simple spectrophotometric assays to monitor the rate of production, or utilization, of NADH.

Creative Approaches to Problem-Solving

Paul Ellwood

The idea that everyone is capable at some level of creative endeavour is a concept that does not seem to sit easily with many students. At the start of an MBA module I teach on creativity and innovation, I invariably hear that students have chosen the elective because they are *"not creative, but would like to be"*. It is also not uncommon to hear *"I originally trained as a scientist (or engineer) and obviously creativity is not something we do"*.

During the course we succeed in dispelling the myth that creativity is a special attribute of a gifted few, dependent on their genius or muse. Beethoven and Darwin are undoubtedly creative giants, but it is important to draw a distinction between the lofty heights of the achievements (i.e. level of attainment) and the creative process itself which might be approached at all levels in a designed and purposeful manner.

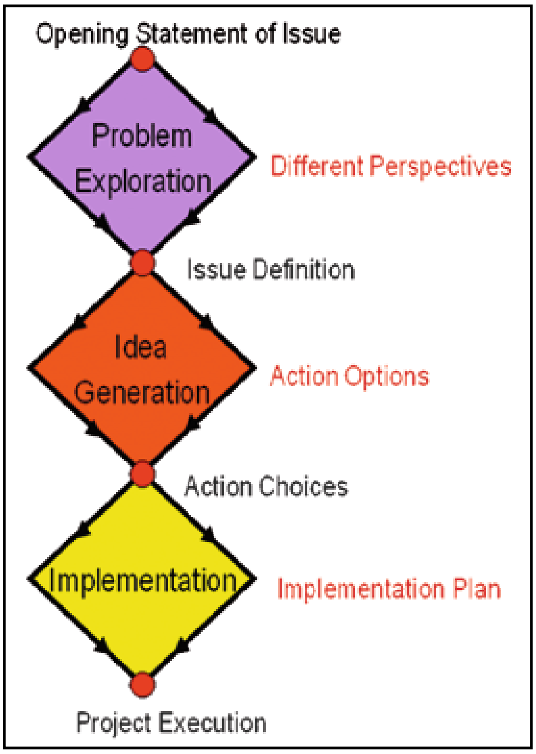
With such an outlook in mind its is useful to take as a starting point a definition of creativity offered by Professor Teresa Amabile of Harvard University (Amabile, 1998). She writes that *"creativity is…the production of novel, appropriate ideas in any realm of human activity from science, to the arts, to education, to business or to everyday life"*. She develops her arguments to suggest that creativity happens at the congruence of expertise, intrinsic motivation and creative thinking skills.

Amabile argues for the domain dependence of creativity; the idea that creativity is only possible following deep experience or immersion in a subject. For example, people trained as historians or in other non-scientific disciplines may well be able to produce ideas on bioscience that we would call *novel*, but they would invariably fall at the *appropriateness* hurdle of her definition of creativity. In addition, creativity is only likely to happen for those people who feel personally motivated to produce a new result. In the context of teaching, and recognising the issue of student motivation is too large a topic to be addressed here, it is worth noting the importance of the lecturer in influencing the learning climate. Studies of creativity in groups (Hunter, 2007) have repeatedly noted the importance of those in leadership positions conveying the value they place on creativity and adopting a nurturing perspective in their interactions.

Whilst factors such as expertise and motivation can only be influenced in part by any one lecturer, promoting creative thinking skills is something that can be tackled more directly by anyone. A large number of books are available that catalogue individual creative thinking tools. These are collections of activities designed to take participants through a number of thinking steps that culminate in new insights or ideas. Whilst building a personal collection of such thinking tools that are varied enough to work in different situations, it is important to have in mind a conceptual super-structure of a creative problem solving process into which individual thinking tools may be placed.

One such 'super-structure' is the classic creative problem solving process developed at the University of Buffalo by Sidney Parnes and (the father of brainstorming) Alex Osborn (see VanGundy, 1987 for an account of the development). This is shown in Figure 1 (see overleaf) in an abbreviated form that is useful in a classroom. It emphasises both the different stages of the process (problem exploration, idea generation and implementation) and distinct thinking phases (divergent and convergent) within each stage.

Figure 1



Starting with some opening statement of the challenge, thinking tools are used to generate different perspectives (divergent phase) on the issue. Judgements (convergent phase) are then brought to bear on these viewpoints in order to settle on a definition of the challenge against which a large number of new ideas will be generated in the next divergent phase of the process. Sorting of ideas typically precedes some decision making (convergent) activity to decide which ideas are going to be implemented. And this final implementation stage may also be viewed as comprising divergent (i.e. planning) and convergent (i.e. execution) phases.

Although space does not permit an account of the richness of this process (see Van Gundy's books in the bibliography for a full account), the relevance of creative thinking skills for generating *novelty* during the divergent phases, and domain-dependent expertise for choosing *appropriate* options may be evident.

Some important practical points to note about the process are that first and foremost, the divergent and convergent thinking phases should be kept separate, in order to allow for sub-conscious incubation of ideas and therefore better decision making. It is also not necessary to follow the process in a linear fashion; it is often better to iterate particular stages as new insights are generated. And one final point to note is that the process, however well executed, will not overcome personal demotivation.

When faced with problem-solving challenges in both a classroom and business setting I have often encountered a number of generic weaknesses in the approaches adopted to seek solutions. An apparent desire to appear decisive and move swiftly to a solution leads to what I call the 'inspired guesswork' school of problem-solving. This involves generating a limited number of options and quickly selecting a preferred course of action. It suffers from no consideration of the nature of the problem, nor the benefits of allowing a larger range of options to incubate in the subconscious. A frequent result is that problems are 'solved' which do not actually exist. By adopting the more purposeful approach outlined in this article, space is made for creativity and the individual contribution of all participants.

References

Amabile, T. (1998) How to Kill Creativity. *Harvard Business Review*, September, 77–87

Hunter, S.T. (2007) Climates for Creativity: A Quantitative Review. *Creativity Research Journal* **19** (1), 69–90

Van Gundy, A.B. (1987) *Creative Problem Solving: A Guide for Trainers and Management*, Greenwood Press

Van Gundy, A.B. (1998) *Techniques of Structured Problem-Solving*, Van Nostrand Reinhold

Case Studies

In the first of these case studies, John Shuttleworth describes an approach that promotes enquiry-based, investigative work at level 2 of a Cell Biology programme. Students are not only introduced to the scientific process/method but are also encouraged to be imaginative and creative in their suggestions for experimental approaches that may be adopted. In the second case study, involving level 3 students, Raul Sutton and Sara Short demonstrate how the skills required to solve both a 'closed' problem, involving a numerical calculation in population genetics, and an 'open' problem in forensic science can be fostered in the context of a criminal investigation. Finally, Carol Wakeford describes how she encourages creative approaches to problem solving by asking groups of students to use a range of creativity tools as they generate novel ideas for their own e-learning projects at level 3.

These excellent and diverse case studies illustrate just some of the very wide range of approaches that may be adopted for the promotion of problem solving skills in the biosciences. We hope that these examples will inspire colleagues and encourage them to submit further case studies to a Centre for Bioscience central resource that will be available to all members of the bioscience teaching community.

Case study 1 CELL BIOLOGY

Developing problem solving and research skills in Medical Science students

John Shuttleworth, University of Birmingham

Background and rationale

Scientific research can be considered as one of the ultimate problem solving activities. The Bachelor of Medical Science (BMedSc) programme at Birmingham aims to produce graduates who are well equipped to go on and undertake postgraduate research. In addition to developing practical skills the course is committed to encouraging enquiry, critical analysis and problem-solving skills. Getting students to think about how knowledge is acquired and communicated, coming up with questions and ways of finding answers, is a key objective. One of the ways in which students are encouraged to develop these ways of thinking is through a compulsory Research Methods course that forms part of a skills module in year 2.

A sound knowledge base, that includes introduction to a wide range of molecular and cell biology techniques, is established during the first and second years of the programme. The Research Methods course creates the opportunity for students to reflect, and think about how these methods can be used to advance knowledge and understanding. By engaging with this course students become more familiar with the intellectual (as opposed to the practical) aspects of the scientific process, in preparation for the heavily research-focussed final year of the programme that culminates with a full-time, 10-week laboratory based research project.

Methods

The rationale and organisation of the Research Methods course is explained in an introductory lecture, which is followed up by a second lecture that explores the thinking behind what can be considered as the scientific process (coming up with a question, formulating and testing a hypothesis, experimental design, analysis and interpretation of data, making conclusions etc). The lecture also looks at the way in which research is communicated in the primary literature (the structure of a journal article, the purpose behind each section, ways to approach reading and extracting key information). Students are referred to the excellent Engage in Research web site developed by the Centre for Excellence in Teaching and Learning in Applied Undergraduate Research Skills (CETL-AURS), University of Reading, UK, [http://www.engageinresearch.ac.uk/].

Discussions with students confirm that they have not necessarily thought much about these aspects of science before, despite explicit reference to this activity in lectures, and having undertaken practicals. First and second year undergraduate practicals are perhaps not as investigative as we would like them to be, and this is another area that the programme is focussing attention on.

The course itself is based on three 2-hour small group problem-solving sessions, scheduled two weeks apart so as to allow sufficient time for students to prepare and fully engage. The sessions are structured around worksheets that explain the rationale for each session and set a number of tasks to be completed by students working in groups of 3-4 before the session. Solutions to the tasks are then discussed and debated during the session. Tutorial group size is around 12-14 students, which means that up to 3-4 different sets of approaches get to be considered.

Session 1: literature review and experimental design

The first session is a ‘brainstorming’ session structured around a worksheet that sets out 2 tasks.

Task 1: A reference to a short journal review article on the structure / function of the p53 tumour suppressor protein is provided. Students must find and download a full-text electronic copy of the article, read it and produce a set of brief bullet point notes that summarise the major key points communicated by the article.

The review article builds on knowledge introduced in Cell Biology lectures, and takes students to another level of complexity where they have to begin to make judgements based on understanding. The ‘problem’ that students face is figuring out what a major key point is (as opposed to minor points). During the discussions it rapidly becomes apparent that without an understanding the information cannot be processed or organised in this way. This activity integrates with literature searching and abstract writing activities that form part of other year 1 and year 2 modules.

Task 2: Having read the review article, students are next asked to formulate the questions they would need to ask, and how they would go about answering them, in order to arrive at the knowledge communicated by the review article. In this case the functions of p53 protein provide a wide range of opportunities to come up with constructive ideas (does p53 protein bind to DNA, in a sequence-specific way, and regulate expression, of which genes etc.).

The ’problem’ here is to come up with focussed questions (not always easy for students, who are more practiced at coming up with answers) and then match these with appropriate experimental approaches. Students know the list of methods, and what they are used for, but have not needed to give much thought to how the parts come together, nor the nature / limitations of the data that can be acquired. As a prompt a list of suggestions is provided, without which students have found it difficult to engage with the problem.

Each of the groups is required to prepare a short report in advance of the session. This forms the basis for active contribution and discussion. Ideas and suggestions come forward and are allowed to accumulate before being discussed and judged (as being good or bad, and for what reasons). Feedback occurs as a natural outcome of the session, as discussions reveal solutions to the tasks. The reports are formatively assessed, and handed back with comments providing additional feedback not touched on during the session.

Session 2: data analysis and interpretation

The worksheet for this session contains data from a series of experiments that have been carried out to investigate p53 structure and function, and logically builds on many of the ideas that emerged during the ‘brainstorming’ of

Session 1. Each experiment is lifted from a different research article, and is contextualised to aid interpretation (sources are not acknowledged to avoid the temptation for students to take shortcuts to the original articles). A series of questions about each experiment forms the basis for the exercise, and structures the thinking necessary to analyse and interpret data. This gets students thinking about how to investigate p53 structure and function (transactivation, specific DNA binding, induced gene expression, activation of apoptosis and protein interactions) and draw conclusions from a variety of different kinds of experiments (recombinant DNA / cell transfection, gene expression, electrophoretic mobility shift assays, immunocytochemistry, affinity chromatography / GST pull-down)

The 'problem' posed by this session relates to accurate interpretation of data. Students commonly over-interpret, and fail to limit their thinking to the experiment being considered, before moving on to integrate the information with that from other sources (this may partly arise from the artificial situation where students are in effect 'retracing steps', with the review article still fresh in their minds). The questions also provide a springboard to launch into more detailed discussions on the logistics of the experiments described and also calling on students' imagination and creativity to suggest other experiments and approaches. Interestingly, many students comment positively on the added dimension that these sessions provide to the previously isolated factual knowledge that they are used to handling.

As for Session 1 a report is prepared by each group. This is handed in at the start of the session, and is summatively assessed, to contribute a relatively small, but significant component towards the module mark. Just as in Session 1, feedback happens as the discussions proceed. Students retain a copy of the report that they have already handed in at the start of the session, so that they can annotate this during discussions.

Session 3: critical reading of primary literature

Students are given a mock-up of a draft research manuscript based on a real draft manuscript, and are asked to take on the role of a reviewer, looking for inconsistencies, omissions and inaccuracies in interpretation of data. The subject of the paper is an investigation into the cellular effects of p21CIP1 expression (p21CIP1 is a protein that is normally induced by the p53 tumour suppressor protein). The investigation uses a genetically engineered cell line that students have themselves used in experiments during Cell Biology practicals.

The manuscript builds on a pre-existing conceptual and factual framework, from lectures and practicals in Cell Biology, and the preceding Research Methods sessions. This in principle gives students an opportunity to focus on solving the problems presented by the paper itself rather than getting up to speed with the background. Hence, this approximates the situation that exists in the research-based final year course when students will be using primary literature sources to extend their knowledge and understanding within the context of taught options and projects.

The manuscript contains some very basic and fundamental flaws that do not require a detailed knowledge of the subject area to spot. Most notably: (1) the design of experiments and their interpretation is flawed, with data from different experiments being compared even though the time points are not the same, and (2) changes in cell diameter are used as a measure of cell growth, when a calculation of cell volume would be more appropriate. A set of structured questions guide students through the process of extracting information, and critically evaluating the study (for example questioning the choice of methods, summarising experimental rationale and confirming the reliability of interpretation of data). Discussions can also explore any difficulties that have been encountered in making sense of the information presented in the paper.

Students have commented that they find the reading of research articles particularly demanding, and critical reading therefore represents a 'problem' that requires solving. By contriving a 'spot the mistakes' exercise the objective is clear and challenging. Achieving the objective requires skill, to recognise the errors and inaccuracies.

Advice on how to use the approach

Session / worksheet content

Judging the appropriate level, and the amount of work required, is crucial if students are to be challenged to reach achievable goals. Finding a comfortable and reasonably familiar starting point allows students to concentrate on the thinking and leave behind the notion that they are doing this to 'learn' more lists of facts. Anticipating how easily the session can develop beyond what is defined by the worksheet will help to add value.

Timetabling

Sufficient time must be allowed between sessions for students to work effectively on the exercises, and prepare their reports. Workload should be evaluated, alongside other commitments such as pending coursework deadlines. The length of each session should allow time for discussion to reach satisfactory conclusion, and is of course linked to the size and complexity of the problem. It has been found that two hours gives the necessary flexibility to bring sessions to a conclusion, although it is rare to use a full two hours as attention begins to wane.

Tutors / Facilitators

The Tutors who facilitate these sessions are for the most part research-active members of staff who also have experience of teaching and interacting with undergraduate students (both in second year and final year taught options and projects). Involving the Tutors in the planning of the sessions has not only helped to establish the content and learning objectives but also ensures a reasonable consistency of approach, even though differences in personal style and group dynamics lead to variations. Tutor notes help to keep the sessions on target.

The unanimous view of Tutors / Facilitators is that the sessions are very enjoyable to teach. The enthusiasm and insight that they bring to the sessions can inspire students.

Student participation

An emphasis is placed on the importance of attendance and contribution. Not only is it important for individuals to work as part of a group when preparing reports, but also they must participate in discussions during the timetabled sessions. It is not easy to grade student participation and contribution meaningfully, and these aspects of performance are judged as pass / fail.

Does it work?

Without a doubt these sessions can lead to changes in the mind-set of students. Course evaluation has been very positive. Some students do struggle conceptually, and others do not work easily as part of a group, but this is to be expected. Disappointingly there are one or two students who fail to see the relevance, or do not think they are receiving adequate feedback, however a majority of students feel that they have enjoyed and benefited from the sessions. Free text comments include:

- enjoyable; relevant; valuable.
- challenging and thought provoking; at the right level.
- welcome change from lectures; offered a different perspective.
- increased confidence; ability to think critically.

A rigorous evaluation of how effective the sessions are, based on assessment, has not been carried out.

Further developments

Fine-tuning of the level of guidance given to students in the worksheets is an ongoing task. The use of set questions to structure student thinking, and give a toe-hold on the exercises, is being reviewed to maximise the problem-solving aspects of these sessions. Ideally students must be given as much opportunity as possible to come up with their own ideas and find the questions themselves, however in the early stages of their training this needs to be balanced against the risk that they are unable to identify the task accurately. It is hoped that a similar approach can be integrated into a wider range of subject areas.

Accompanying material

Examples of the worksheets, handouts and Tutors notes, together with a summary of a recent course evaluation, are available from the accompanying web site (http://www.bioscience.heacademy.ac.uk/resources/problemsolving/).

Acknowledgements

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Case study 2 GENETICS/FORENSIC SCIENCE

Contextualising genetics using forensic science

Raul Sutton and Sara Short, University of Wolverhampton

Background and rationale

Problem-solving is seen as an essential skill that is developed in biology education. Thus from GCSE biology [OCR, 2008] the need to problem solve is embedded in the syllabus objectives via the following objective:

plan a scientific task, such as a practical procedure, testing an idea, answering a question or solving a problem;

This is then developed at key stage 5 as the OCR, GCA AS/A2 Biology syllabus defines in its objectives (OCR, 2002):

"apply biological principles and concepts in solving problems in unfamiliar situations including those which relate to the ethical, social, economic, and technological implications and applications of biology".

The expectations of problem solving are articulated in University curricula via the QAA subject benchmark for organismal and cellular biosciences (QAA, 2007):

"the ability to think independently, set tasks and solve problems."

The way in which people solve problems has been articulated by Newell and Simon (1972) as being of three elements: a problem state, which defines the problem, a search space, which is all the information that might be used to find a solution and finally a goal state, which is the solution. The solving part can be seen as the bit between the problem state and goal state. Within this there must be some consideration of the variety of problems that can be asked of the student and these range from a simple closed problem such as the application of the correct equation to a numerical problem to open-ended problems where there are a number of strategies that could be employed to solve the problem and the time frame may require a flexible and dynamic response to these problems. The latter is often typical of the workplace environment, where the demand may not always be couched in the terms of pure science but may require interim solutions, evolving investigation strategies and modified outcomes based upon a shifting goal. Between these two there is a large range and good educational practice will look to develop the learner towards dealing with the latter by providing a range of problems to solve.

Within biology the application of population frequency data is often presented in abstract forms without contextualisation. One aspect of population dynamics that is clearly contextualised is the use of allelic frequency databases for assessing the likelihood of having obtained a matching result by chance in DNA profiling [Butler, 2001]. In DNA profiling, population frequency datasets are used to calculate the likelihood of a particular piece of DNA-rich evidence originating from a source unrelated to the suspect by random chance. The DNA sample from the crime scene is processed by PCR amplification of regions of DNA that contain short stretches of repeating DNA, known as short tandem repeats. The number of the repeats will vary between individuals so that the amplified region will vary in length depending on the number of repeats. The amplicon is genetically determined and comparison with a database of population data will allow a calculation of the frequency of the amplicon within a population group. For the UK population, frequency databases have been compiled for three ethnic groupings (Evett, 1997) for ten different allelic regions (Foreman and Evett, 2001]. For worldwide frequencies more complete dataset exists [http://alfred.med.yale.edu/alfred/index.asp).

The reason why these datasets have applicability is the estimate of value of matches obtained from searching databases of individuals' DNA profiles and DNA profiles from samples from crime scenes. Samples identified as having similar allelic makeup can then be shown to have a low probability of having come from someone other than the donor by random chance. In the UK, until recently, all persons arrested for indictable offences had a sample of their DNA taken and this was added to the national DNA database. In 2009 the European Court of Human Rights ruled that DNA taken from persons that were subsequently acquitted should be removed from the database (Gillan and Quinton vs The United Kingdom, 2009). This will result in the database being reduced in size from about 4.5 million persons by about 800 000.

Methods and advice on how to use the approach

The problem is set within a third year undergraduate forensic science course, where the student is to get the experience of acting in the role of a courtroom expert, based upon a request for sample analysis from a local constabulary. The students have previously undertaken a second year forensic biology module that includes the basics of the use of DNA in a forensic context which has built on an introductory molecular biosciences module studied in the first year.

The forensic context can be used to allow students to experience realistic case scenarios and act in the role of a forensic case worker and expert witness. This was achieved by:

1. utilising a series of crime scenarios from which key evidence has been gathered;
2. creating a dataset of DNA profiles for a group of 'suspects' and 'victims';
3. creating a set of crime scene samples which the student can analyse for DNA profiles;
4. creating a realistic timeframe to allow the student to role play analysing and requesting a DNA profile analysis from a crime scene sample;
5. allowing the student to analyse the profile against a matching profile gathered from the witness and suspect in the 'case';
6. present the results in a formal report for court;
7. present their findings orally in court as an expert witness under cross examination.

Many of the skills that are used here form part of the Forensic Science Society's 'Interpretation and Evaluation of Evidence' component standard that forms part of its accreditation process for university courses (Forensic Science Society, 2008).

1. The Cases

The cases were all related to material that had been gathered at 'mock' crime scenes that the student experienced in their second year of study. In all six different cases were created, each with one suspect and one victim. For each case there was a description of a modus operandi contained in a 'Laboratory Submission Form' (see appendix 1 http://www.bioscience.heacademy.ac.uk/resources/problemsolving/ for an exemplar) that formed the basis of the reason for obtaining a DNA profile from the sample. From these six cases there were forty two DNA rich samples that the student should have recovered from the crime scene when undertaking this exercise in their second year. These ranged from hair containing the root, through to cellular material (from the rims of glasses, bottles or cans) to semen (stained clothing or on condoms etc.). An exemplar of one of the items is shown in appendix 2 (http://www.bioscience.heacademy.ac.uk/resources/problemsolving/).

2. The dataset containing the DNA profiles

Full and partial DNA profiles were constructed for the DNA-rich evidence contained within each of the items submitted for analysis. These were returned to the students as a 'DNA STR Profiling results: SGM + form'. An exemplar of this can be seen in appendix 3 (http://www.bioscience.heacademy.ac.uk/resources/problemsolving/). Typically, if the student has chosen the correct areas to analyse (see later), these will contain a DNA profile matching the victim and the suspect in the case. For simplicity, it was decided against giving the students mixed profile samples to analyse. Students then had to calculate match probabilities based upon the data that they had received. In order to simplify this step students were asked to do this via simple Hardy-Weinberg methods without correction factors for inbreeding, limited gene pool sizes etc and size bias correction factors. The allele frequency dataset that they used were the UK 3 ethnic group datasets (Caucasian, afro-Caribbean, and Asian) based upon the 10 locus SGM+ method for DNA profiling. Calculations would then result in the student choosing the most common match probability when presenting their analysis in their court report (i.e. the probability that is most favourable to the defendant). The calculated match probability varied between 1 in 10^4 and 10^9. depending on which sample was analysed.

3. The crime scene 'samples'

These have been described earlier and an exemplar is shown in appendix 2.

4. The timeframe

Students were given introductory lectures on the subject and then each student was assigned a case and exhibit, with two samples to be analysed for each scenes of crime exhibit. These cases, which contained the materials shown in appendices 1 and 2, could be uploaded by the student. The last page of the form in appendix 1 is a submission for analysis sheet. Students had to complete the sheet within 7 days. Each sheet was individually examined by the module team and an appropriate DNA profile result returned to the student (normally within 48 hours by email). This aspect of the task was made more realistic by submitting a return relevant to the submission request. For example, the garment shown in appendix 2, which was recovered form the crime scene, in this case the victim's flat, is likely to have been worn by the suspect. There are two blood stains on the garment. The case notes contained within the file given to the student contained detailed examination notes for their crime scene exhibit. Those notes included the results of any presumptive stain testing that had been done. They were therefore expected only to choose DNA profile analysis by the SGM+ methodology. Students who asked for each of the blood stains to be analysed will have received back a DNA profile that matched the victim, but will not have got back a profile matching the suspect. A good source of suspect DNA will have come from areas where the suspect's skin had been in contact with the garment, such as the elasticated cuff, or inside where the collar abrades the neck. Students who requested these samples would also receive a partial DNA profile matching the suspect and the full DNA profile of the suspect as recovered from the DNA database. Request for analysis of both suspect cellular material and bloodstains yielded profiles matching both victim and suspect.

Students were allowed to submit a second request for analysis if they did not get the necessary results from the first sample, but it affected their grade (unnecessary use of budget and wasting time). Students who submitted requests for too many analyses to be performed were told that the budget would not cover so many sample requests. Students had 2 weeks in which to resubmit samples, if necessary, conduct DNA profile analysis and prepare their statements for court. This gave some realistic feeling of the sort of time pressure that is encountered in the workplace.

5 and 6. Profile analysis, Evidence Interpretation and Court Report

Once the student had noted that the partial profile obtained from the crime scene exhibit matched the corresponding parts of the suspect's full DNA profile revealed from the database they used the allele frequency charts to calculate match probability data. For simplicity, no correction factors were used and the students were asked to present the results in terms of simple Hardy-Weinberg methodologies. The working for these would form one of the appendices for the report (see earlier). The students had already been told on the additional submission form what race code the suspect was. However, regardless of the race code of the suspect they should still choose, for mention in their statement, the most favourable race code out of the three that they had calculated.

Students were advised to use a Bayes Theorem approach to interpretation of the evidence (Jackson *et al.*, 2006). The supporting lectures introduced the students to the idea of the hierarchy of propositions (Cook *et al.*, 1998) so that they had to decide whether to interpret their evidence at sub source level, source level or activity level. For activity level interpretation the student could ask the 'Senior Officer' in the case for information regarding the suspect's version of events.

Students could then use the results in a report to be written in a style suitable for the courtroom. Again guidance was given on how to present the results, with due respect to relevant case law and in terms of a style suitable for the court as well as to get the citing of the statistical part of the court report correct. In particular, students received some tuition on avoiding 'the prosecutor's fallacy' (Balding and Donnelly, 1994; Evett, 1995).

7. The Expert Witness Oral Testimony

The court reports were used to construct for each case a series of questions that could be used for cross-examination purposes in a moot court scenario. The questions ranged from simple questions asking the student to describe DNA profiling in 'layman's' language (surprisingly difficult to do without proper preparation and in depth-understanding) through questions about the calculated probabilities through to questions relating to the activities that could have caused the sample to have been present in the crime scene. Cross-examination was carried out by final year LLB students who were experienced at mooting, one for prosecution and defence using the University of Wolverhampton's School of Legal Studies mock court room. Each of these advocates would have a series of questions set by the module team that were equivalent and case specific.

8. Student assessment

Students were assessed on all aspects of the process management. This included time management (via submissions to deadlines), quality of the written report (where the application of the biology was assessed) and the court room presentation.

Advice on troubleshooting

There are some teething problems that we have encountered that the user will have to take into consideration. These are:

1. How to treat students that do not submit a sample for analysis.

   The success of this module relies heavily on student engagement. Our experience has shown that students have relished, but maybe have been a little in awe of, the assessment task. We have tried to solve the non-submission of laboratory analysis forms whilst keeping the context by creating a standard letter from the senior investigating officer. This letter asks for their of match probabilities in their expert opinion and asks why results of DNA profile analysis has not been received. This letter goes out the day after the submission of analysis requests goes in to keep the momentum. Students will be deducted marks for late submission in order to compensate for a failure of this aspect.
2. Return of completed laboratory submission sheets.

At the moment these are returned the day after the forms have been handed in. This means that each form has to be checked and the appropriate analysis constructed, which is time consuming in the short term. There are students who fail to make adequate requests for sample analysis mainly due to either the wrong area on the sample chosen for analysis or too many areas chosen for analysis. For the former they get the DNA profiles that are suitable for the area chosen. If the area does not get suspect DNA they will have a 'negative' search of the 'National DNA database' for suspect profile. These students will be allowed to resubmit after extra advice and grade will be mediated accordingly. For students who choose too many areas we have chosen to return their form with a request that they narrow the number of DNA profile requests as their budget will not allow them so many analyses. For a few students this means that at this stage there is regular email traffic.

3. Failure to submit a court report.
   Again reminders are sent by email. Students who continue not to submit court reports are not invited for cross examination and fail the assessment. In the current cohort of 45 students, only one was in this position.
4. Failure to attend to give oral testimony.
   Students are invited to give oral testimony at a specified time. Each oral testimony takes about 10 – 15 minutes. Students who do not attend at a specified time are failed but given a chance to be reassessed in this part of the module at a later time. There is some flexibility at this stage with respect to short term absence, as the cross examinations take place on 3 consecutive weeks on the afternoon that the module operates on.
5. Creation of question banks for oral testimony.
   This caused a problem in the first iteration of the module. This was because each sample that the students had was different. This meant that a different set of questions was created for each student. This problem was exacerbated by tailoring questions in the first iteration of the module to the court report. We resolved this issue to some extent by keeping the case specific questions whilst removing the report-specific question. Although not ideal, as in real court questions would be directly related to the written court report, it was seen as the best way to manage the large number of students undertaking this module.

Does it work?

There are two types of problem solving issues that are embedded within the exercise described here. The first is very much of the 'closed' problem type with the students having to calculate a numerical solution to a problem based on population genetics. The methodology is relatively straightforward, in this case only being complicated by the fact that it was a partial DNA profile, the need to calculate for each ethnic group and in choosing the match probability most favourable to the defendant. The second problem that the students have to deal with is the much more open issue about the range of activities that caused sample deposition and this is very much a matter of individual interpretation with a number of possibilities for these events. This is much more difficult for the students and has been more discriminatory in terms of its assessment.

Students often study heritability and population genetics in isolation. Although the theory of population genetic frequencies is relatively straightforward and the datasets reasonably well established, the relevance of this is not always apparent. Placing the population statistical approach in the context of forensic casework enabled the student to see the applicability of the science to societal situations. The calculation of match probability was used in the preparation of the court report. This 'source level' interpretation gave very high match probability or likelihood ratios in general. Students would then have to apply those probabilities to the case in question in order to hypothesise the type of activity that could have led to the sample being present in the crime scene. Good students would be able to rationalise a number of likely scenarios to explain the evidence and opine on which was the most likely from the nature of the sample. In all of these, the probable identity of the source DNA was not questioned but the method of its deposition was what concerned the court. In this the underpinning genetics becomes less important than activity causing the deposition, which was something that most scientists are not aware of until they see the role of their science in a wider context.

The exercise in itself also tested a range of transferable skills. For the students a glimpse at the role of a professional forensic scientist made them more aware of the daily pressures experienced by the laboratory worker and some of the key differences between being a DNA analyst and an expert witness. In this, performing to tight schedules in order to meet deadlines gave the student some sort of preparation for the workplace environment.

There were some weaknesses in the approach that should be reviewed. The first is how to provide much greater information about the case, such as other witness statements and closer contact with the Senior Investigating Officer so that the students can make a better activity level interpretation. Our intention is to address this in future by having additional generic supplementary information available on request.

In addition, although the risk of collusion is reduced by offering the students individual samples to analyse, there is a chance that previous year students could inform current students about their calculated match probability.

Further developments

A further development that is being considered is the development of the current materials into an interactive software programme. In this the software would manage most of the case with more realistic timeframes being built into the system. In addition, there would be scope for the design of random partial profiles based upon the frequency information stored in the dataset, so that every student would receive a 'unique' profile with the software automatically calculating the match probabilities. Students would then have the opportunity to check their results by entering their calculated match probabilities into the software. The number of times before the student entered the correct match probability would be used in calculating the student grade. There would be opportunities to build in additional presumptive testing and a costing element for students could be introduced to the system to allow for realistic estimation against budgets.

References

Balding, D. and Donnelly, P. (1994) The Prosecutor's fallacy and DNA evidence. *Criminal Law Review* 711-713

Butler, J.M. (2001) *Forensic DNA Typing* Academic Press

Cook, R., Evett, I.W., Jackson, G., Jones P.J. and Lambert J. A. (1998) A heirarchy of propositions. Deciding which level to address in casework. *Science and Justice* **38** 231–239

Evett, I.W. (1995) Avoiding the transposed conditional. *Science and Justice* **35** 127–131

Evett, I.W. (1997) Statistical analysis of data for three British ethnic groups from a new STR multiplex *International Journal of Legal Medicine* **110**, 5–9

Foreman, L.A. and Evett, I.W. (2001) Statistical analyses to support forensic interpretation for a new ten-locus STR profiling system *International Journal of Legal Medicine* **114** 147–155

Forensic Science Society (2008) Component Standard. Available at www.forensic-science-society.org.uk/Resources/Forensic%20Science/AJINTERPRET%20amend161108.pdf (accessed 13th May 2009)

Gillan and Quinton v. The United Kingdom (2009) Available at www.echr.coe.int/ECHR/EN/Header/Press/Multimedia/Webcasts+of+public+hearings/webcastEN_media?&p_url=20090506-1/en/ (accessed 13 May 2009)

Jackson, G., Jones, S., Booth, G., Champod, C. and Evett, I.W. (2006) The nature of forensic science opinion — a possible framework to guide thinking and practice in investigations and in Court proceedings. *Science and Justice*. **46**(1) 33–44

Newell, A. and Simon, H. A. (1972). *Human problem solving*. Englewood Cliffs, New Jersey: Prentice-Hall

OCR (2002) OCR AS GCE *in Biology (3881) OCR Advanced GCE in Biology (7881) Approved Specifications – Revised Edition*, OCR, p15

OCR (2008) OCR *GCSE in Biology* B J643, OCR, p106

QAA (2007) *Biosciences*. Available at www.qaa.ac.uk/academicinfrastructure/benchmark/statements/Biosciences07.pdf (accessed 13 May 2009)

Case study 3 GENERAL: CREATIVE THINKING

Students generate ideas for e-learning projects/ resources

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Background and rationale

A proportion of Final Level students in FLS opt for e-learning projects, in which they design and develop online resources, usually to support the undergraduate curriculum. Recent funding from the University CETL, the Centre for Excellence in Enquiry-Based Learning (CEEBL) has lead to attempts to marry e-learning with EBL, and part of the remit for project students is to produce e-resources with a focus on stimulating enquiry by their target group. However, project students were intent on conveying as much information as possible via their resource, and found it difficult to focus on learning design rather than content alone.

The problem then was how to encourage students to create more imaginative learning designs that would promote the skills of enquiry (asking questions, research, critical thinking) in the target group.

This is an example of a student-led, open-ended problem.

Methods

Traditionally, students opting for e-learning projects attended a training course to equip them with appropriate project skills. Topics included project planning, critical review of online resources, IT skills, copyright issues, and project evaluation and statistical analysis (Wakeford, 2008). In an attempt to improve creativity in the design of the e-learning resources additional sessions have been included in the training course. Students work in groups of 6-8 and use a range of creativity tools to facilitate the generation of ideas for their learning designs. To monitor proceedings, a chairperson is elected, who is responsible for time-keeping, and for ensuring that the generation of ideas is not interrupted by premature discussion; selection and discussion of ideas is carried out *after* idea-generation, and continues in online groups to allow for a period of 'incubation'. In addition, a scribe is selected to record ideas where appropriate.

Creativity tools (Bransford and Stein, 1984; Isaksen *et al.*, 2000) include:

Lateral thinking exercises: puzzles to help students think-outside the box' in preparation for group work.

Traditional Brainstorming techniques (or 'thought showers'): students generate ideas at random in a group. The usefulness of ideas is subsequently evaluated; this is known as deferred judgement. Ideas can be recorded by the scribe, or by individuals on post-its.

Brainwriting: this is a modified version of brainstorming, where participants record 3 ideas each on a proforma. The proformas are then placed in the centre of the group and redistributed. Participants add a further 3 options, and so on until the sheets are completed. Brainwriting allows individuals more time to consider options.

Random Words: a list of 60 random words is used to trigger the generation of ideas (de Bono, 1996). One member of the group looks at the second hand on the clock and the corresponding number is used to select a word from the list. The Random Word itself is classed as the initial stimulus. A Bridging Idea is then established, which is based on the stimulus. This idea then acts as a bridge between the stimulus and a new idea related to the problem.

Example: A random word Bikini is selected in relation to solving a car-parking problem (too many cars and not enough spaces). The bridging idea is that a bikini has 2 parts. This is now applied to the problem – consider a 2-story car-park, or car sharing between 2 people etc. (de Bono, 1996).

Visual prompts: a selection of postcards is used to prompt students to reflect on their own (good and bad) experiences of learning.

SCAMPER: an acronym useful for considering different aspects of the problem (resource) in order to modify and improve the design. It comprises a series of focused questions that facilitate reflection on and evaluation of a problem:

Substitute (what else could we do/use?)
Combine (how about a blend/combination?)
Adapt (what could I copy?)
Modify (what could I change?)
Put to other uses
Eliminate ("less is more")
Rearrange or reverse (what if items are interchanged, transposed etc?)

Attribute listing
Break the object, problem or task down into the component parts and address these elements separately (e.g. mode of presentation, content components, assessment, target group etc). The attributes are compiled into a table, where they form column headings. Variations on each attribute are listed in each column under the appropriate heading, and then different attributes are selected across the rows of the table, to generate novel combinations.

Mind-mapping: to carry forward potentially useful ideas.

Online group discussions to allow a period of incubation (selection and consolidation of ideas). These are then mapped out individually.

Advice on how to use the approach and on troubleshooting

I have found that many students are reluctant to engage in creative thinking activities and need to be prepared:

- Ice-breaker activities help to socialise groups and relax students before creativity work. For example, in 'people-bingo', students have a bingo card that has to be completed by finding a colleague who satisfies the criterion on the card, such as 'A Manchester United supporter'!
- Students need to be aware of the role of the chair and scribe, and the importance of being 'free' to make suggestions, no matter how 'useless' they might think they are!
- It is helpful to give examples beforehand of how each technique might be used. De Bono (1996) illustrates the methods he describes with interesting anecdotes.
- Give students time to 'get-going' with these techniques – they may be reluctant to 'think-outside-the-box' initially.
- Give students the opportunity to reflect on ideas that they might carry forward.

Does it work?

Although a notable fraction of students remain determined to write a text-book for the web, there has been a marked improvement in innovative designs for e-resources since the training course was modified. Student creativity is not generally encouraged by the traditional unit / module presentation via lectures and end of unit examinations, so students need time and assistance to adjust their mode of thinking about problems to a more imaginative way.

Accompanying material

Bransford, J. D. and Stein, B. S. (1984) *The Ideal problem solver*. New York: W. H. Freeman and Co.,

De Bono, E. (1996) *Teach yourself to think*. London: Penguin Books

Isaksen, S. G., Dorval, K. B., Treffinger, D. J. (2000) *Creative Approaches to problem solving: A framework for change*. Kendal/Hunt Publishing Co., USA

Wakeford, C. (2008) Student Research Projects: guidance on practice in the biosciences, Centre for Bioscience report (case-study of FLS e-learning projects)

Creativity in the Biosciences: www.bioscience.heacademy.ac.uk/events/themes/creativity/index.aspx

www.fbs.leeds.ac.uk/creativity/php/login.php

Random words: www.randomwordgenerator.com/randomwordtutorial.html

Examples of approaches/ questions used to promote problem-solving skills

The following are three examples of short exercises used to promote problem solving skills. As with the case studies we have deliberately chosen examples that differ markedly to illustrate the diversity of approaches that may be adopted. Once again, we hope that colleagues will be prepared to submit problem solving exercises to a central repository so that the Centre for Bioscience may facilitate sharing of diverse, good practice amongst members of our community.

1. Tina Overton, University of Hull

We shed our skin completely approximately every three weeks.

(a) What weight of skin do we lose during this time?
(b) What does this imply in terms of molecules of amino acid incorporation into the skin per second?

Students can solve this in 20 minutes of so. I don't let them use calculators. Estimate surface area and thickness of skin and then the problem can be solved using the approximate volume or mass of a simple amino acid unit. This gives staggeringly large values for amino acid unit incorporation per unit surface area and tells students a lot about the rate of biological activity.

2. David Adams, University of Leeds

This is a problem used previously as an exam question for final year microbiologists and now used as the basis of a problem-solving seminar:

You are a microbiologist working for a large pharmaceutical company. During routine sub-culture of a filamentous fungus on growth medium in an agar plate you note the presence of an apparent bacterial contaminant. Growth of the bacterium is strongly inhibited in the vicinity of the fungal colony. Your employer appoints you leader of a team of biologists, chemists and biochemists who will investigate this effect. Describe the approach you will take with emphasis on the microbiological aspects of the work for which you have full responsibility.

During the investigation chemists purify an antibacterial agent with a molecular mass of 647 daltons. They ask you to determine the minimum inhibitory concentration (MIC) for this compound against a range of microorganisms of your choice. Describe how you would do this, outlining any pitfalls you may encounter during the work.

Your preliminary results indicate an MIC of 20 $\mu g\ ml^{-1}$ for the activity of the novel antibiotic against an important bacterial pathogen of humans. Indicate whether you consider this level of inhibition to be significant given that MICs for established antibiotics against this pathogen (published in the scientific literature) range from 50 μM to 2 mM. Provide an explanation for your conclusions.

Finally, describe strategies that your team might adopt to produce improved drugs based on your novel lead compound.

The approach adopted in the seminar based on each of the above four paragraphs:

Describe the approach you will take with emphasis on microbiological aspects of the work for which you have full responsibility.

- *Obtain pure culture of fungus producing apparent antibiotic*
- *Identify bacterium inhibited by antibiotic*
- *Check reproducibility of effect*
- *Growth curve: is the antimicrobial a primary or secondary metabolite? - plot log cell no./biomass x time*
- *Optimise growth conditions for production of antibiotic (pH, temperature, batch vs. continuous culture etc.)*
- *Develop bioassay to enable purification of compound by chemists/biochemists*
- *Chemical characterization/full identification of compound*

Describe how you would determine the Minimum Inhibitor Concentration (MIC) for the novel antibacterial against a range of microorganisms - indicate pitfalls you may encounter.

- *Choice of organisms: should include G+, G- bacteria, anaerobic and aerobic bacteria (indicate problems associated with growth of anaerobes in lab.), range of commensal organisms, range of pathogens, fungi? (some antibiotics produced by fungi are active against other fungi)*
- *Need to sterilise compound - may be heat labile, therefore filter sterilise*
- *Artefacts associated with MIC determinations e.g. components in growth media may interfere with assessments therefore need to use range of growth media*
- *Need to use well-defined compound(s) as control under same lab. conditions*
- *(Pure compound may have limited solubility)*

Minimum Inhibitory Concentration (MIC).

Preliminary results indicate MIC of 20 μg ml^{-1}

This is equivalent to 20 mg L^{-1} or 0.020 g L^{-1}

The antibacterial agent has a molecular mass of 647 daltons

In 1 L of a 1 M solution of the antibacterial agent there will be

647 g i.e. 647 g L^{-1}

$\therefore$ *by proportion: 0.020/647 = 3.09 x 10^{-5} M = 0.0309 mM* $\cong$ ***30.9 μM***

The MICs for established antibiotics range from 50 μM to 2 mM

i.e. the MIC for the novel antibacterial is lower, and therefore better, than the MIC for the established antibiotics

Describe strategies that your team might adopt to produce improved drugs based on your novel lead compound.

- *Detailed pharmacokinetic and toxicity studies, coupled with structural and mode of action investigations, leading to production of improved synthetic or semi-synthetic compounds*
- *Related natural compounds from related strains, species?*
- *Select for over-producing strains/use mutagens (indicate pitfalls associated with mutagenesis)*
- *Characterise pathway for antibiotic production*
- *Directed mutation of genes encoding enzymes involved - this could be coupled with expression of gene encoding antibiotic at high levels in alternative host organism*

3. Martyn Chidgey, University of Birmingham

Cells in their social context: knockout of a cell adhesion molecule

Summary

The creation of knockout animals has revolutionised the understanding of how molecules function in the context of living organisms. Through gene targeting the potential exists to generate mice of any desired genotype, and so study the role of any given protein during development and in post-embryonic life. The aim of this session is to look at how knockout mice are produced, and examine some of the ways in which the phenotype of the knockout animals is characterised. For the purposes of this session we shall assume that the target gene encodes an adhesion molecule that is expressed exclusively in the epidermis and oral mucosa.

Homologous recombination

The creation of a knockout mouse depends on the intrinsic ability of cells to mediate recombination between homologous DNA sequences. This allows the investigator to target exogenous DNA (the targeting vector) to a specific site in the genome (the target gene). The targeting vector is designed to disrupt the coding sequence of the target gene (so preventing the production of its protein product) following homologous recombination. In normal cells homologous recombination (also known as general recombination) is essential for DNA repair and accurate chromosome segregation during meiosis.

The targeting vector

The first step in the production of a knockout animal is the construction of a targeting vector. Many different types of targeting vector have been described. In the example shown in Figure 1, the vector is designed to disrupt the target gene by replacing exons 1 and 2 with unrelated DNA. So-called 'regions of homology' are cloned into the vector: these target the vector to the target gene when the vector is transfected into cultured cells. Thus DNA from the 5' side of exon 1, and DNA from the 3' side of exon 2, is cloned into the vector on either side of a bacterial gene called neo, which encodes resistance to the antibiotic G418. This means that when the vector is transfected into cultured cells and undergoes homologous recombination with the cell's DNA, exons 1 and 2 of the target gene are replaced by neo. It is important to understand that only one allele of the target gene is disrupted by this procedure: the other allele is unaltered.

The procedure for generating a knockout mouse

An outline of the protocol used to generate a knockout mouse is shown in Figure 2. Embryonic stem (ES) cells are used because they are pluripotent i.e. they retain the ability to differentiate into all the cell types found in the body, including germ line cells. Briefly, ES cells are transfected with the targeting vector in a dish. It is not possible to successfully transfect 100% of the ES cells in the dish, so successfully transfected cells are selected by adding G418. G418 kills untransfected cells, but those that have been successfully transfected survive (because of the presence of the neo gene) and start to grow as colonies in the dish. Each colony (clone) is expanded and then screened to determine whether homologous recombination between the vector and ES cell genomic DNA has occurred. Screening is necessary because homologous recombination is a very rare event: it is typically detected in about 1 in 50 G418 resistant clones. In the majority of clones vector DNA randomly integrates into the ES cell genome: these clones are of no further use and are discarded. Once a clone that has undergone homologous recombination has been identified it is again expanded, and the cells are injected into mouse embryo (at the blastocyst stage). The injected embryo is then is implanted into a foster mother. Chimeric pups (i.e those that are made up of a mixture of cells derived from both the injected embryo and the transfected ES cells) are identified by coat colour. For example if ES cells from a black mouse are injected into a white mouse embryo, then chimeric pups will be black and white. Chimeric mice are bred with an unrelated white mouse: any black pups from this mating will be derived entirely from ES cells and each cell in their body will contain one normal target gene allele (the + allele) and one disrupted target gene allele (the – allele). The final step is to interbreed black heterozygous (+/-) mice.

Questions

1. The first litter from the interbreeding of two heterozygous animals has been born. To identify the genotype of the offspring you prepare genomic DNA from tail clips, digest the DNA with the restriction enzyme BamHI and carry out a Southern blot (Figure 3) with a radioactive probe. Explain how Southern blots work. Then, using the information provided in Figure 1 identify the genotype of the animals in this litter. (+/+ = wild-type, +/- = heterozygous, -/- = knockout). Explain why some lanes on the blot have two bands whilst others have only one.
2. What can you say about the role of the knockout gene product in embryonic development from the data provided in Table 1 and your knowledge of Mendelian genetics.
3. What techniques would you use to confirm the absence of the knockout gene product in -/- animals. Explain how they work.
4. What can you say about the likely role of the knockout gene product and its distribution from the haematoxylin and eosin (H & E) stained sections of epidermis provided (Figure 4).
5. Although born at the same size -/- mice grow less rapidly than their normal littermates and at weaning are on average 50% smaller. Can you think of any reasons why this might be so?

Figure 1 The targeting vector

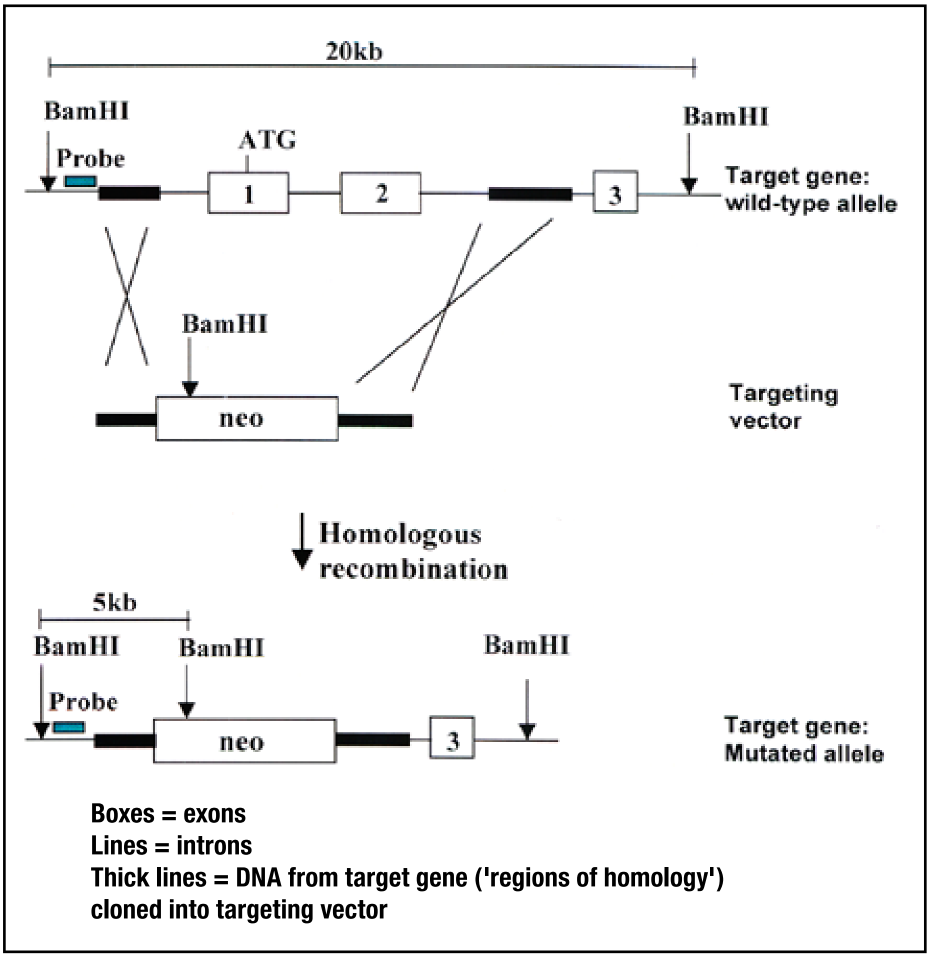


Figure 2 Generation of a knockout mouse

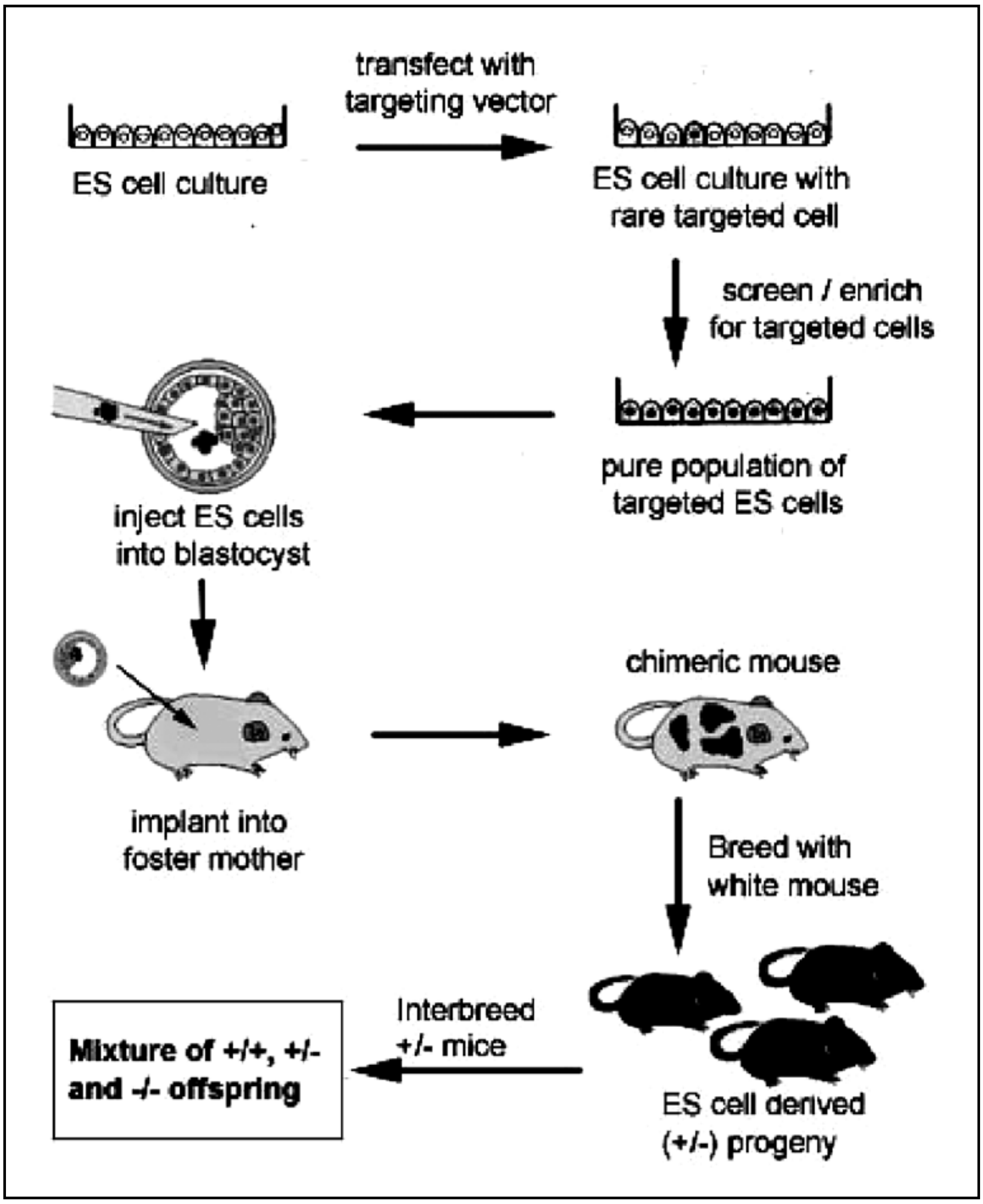


Figure 3 Southern blot

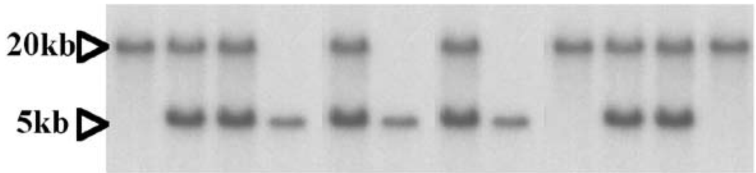
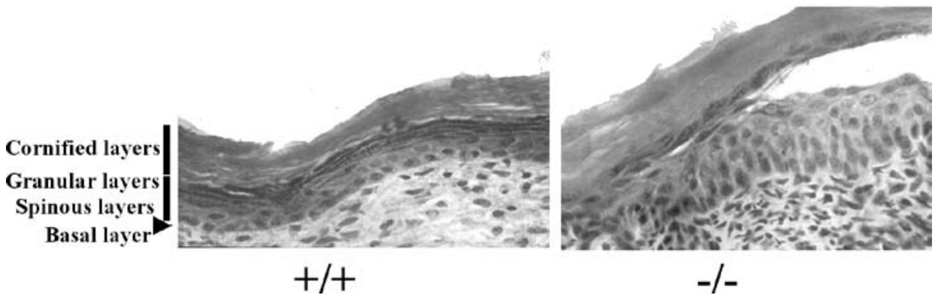


Table 1			
Number of offspring	**39**	**77**	**34**
Genotype	+/+	+/-	-/-

Figure 4 H&E stained sections of epidermis



TUTOR NOTES

Question 1

Southern blotting. DNA is digested with a restriction enzyme and fragments are resolved by agarose gel electrophoresis. DNA is negatively charged so it migrates toward the positive electrode in the electrophoresis tank. After separation, the DNA is transferred to nitrocellulose by capillary transfer. The membrane is blocked (often with sheared, denatured salmon sperm DNA) prior to incubation with a radioactive DNA probe. To label a probe the DNA is denatured, each strand is then labelled by incorporation of a radioactive nucleotide (often [32P]dCTP) into a complementary strand which is initiated with random hexamers and elongated using Klenow fragment.

20kb is wild-type band, 5kb is knockout band. Only one band in +/+ and -/- lanes because the two alleles are identical.

Question 2

1:2:1 ratio so absence of knockout gene product has no effect on embryonic survival.

Question 3

- Northerns
- RT-PCR
- Westerns
- Immunofluorescence microscopy

Question 4

The gene product is a cell-cell adhesion molecule that has an important role in the maintenance of epidermal integrity as epidermal splitting occurs in its absence. It is most likely restricted to, or most strongly expressed, in upper (granular) layers of the tissue where the loss of adhesion between keratinocytes occurs.

Question 5

Feeding defects due to blistering of oral mucosa.

Water loss/infection due to loss of integrity of the skin.

As the blistering occurs in the upper layers and is relatively localised the defect is comparatively mild and only causes some minor loss in the barrier function of the skin. Mild defects in the skin barrier are often counterbalanced by keratinocyte hyperproliferation and epidermal thickening (which accounts for the increased thickness of the epidermis in the -/- section) whereas a more severe defect would result in dehydration and death.

Other questions that you might ask:

- **What could the knockout gene product be?** Either desmoglein 1 or desmocollin 1 – these are both desmosomal cadherins that are most strongly expressed in the upper epidermis.
- **What human disease resembles that seen in the skin of ko mice?** Pemphigus foliaceus (PF) – an autoimmune skin blistering disease that is caused by pathogenic autoantibodies against desmoglein 1. In PF blistering occurs in the upper epidermis and resembles that seen in the ko mouse.

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